# B-type natriuretic peptide in reversible myocardial ischaemia

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SHORT REPORT

# B-type natriuretic peptide in reversible myocardial ischaemia

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**Background:** Coronary heart disease is associated with increased B-type natriuretic peptides (BNPs), and, although controversial, may cause exaggerated exercise-induced BNP secretion. We investigated BNP in relation to reversible myocardial ischaemia.

**Materials and methods:** Serum N-terminal proBNP (NT-proBNP) was measured before and after an exercise electrocardiogram test (ETT) in 14 patients with and 45 patients without exercise-induced myocardial ischaemia. Statistical analysis was carried out on logarithmically transformed data. Results, however, are pre-transformed data.

**Results:** NT-proBNP increased with exercise both in ETT-positive patients (mean (SD) 71.4 (41.2) *v* 76.8 (44.0) ng/l; $p<0.001$) and ETT-negative patients (54.0 (61.2) *v* 60.1 (69.0) ng/l; $p<0.001$). Pre-exercise and post-exercise NT-proBNP were higher ($p<0.05$) in ETT-positive than in ETT-negative patients. Incremental NT-proBNP was similar in ETT-positive (4.7 (4.2) ng/l) and ETT-negative (6.2 (8.6) ng/l) patients.

**Conclusion:** Serum NT-proBNP concentrations are higher in patients with exercise-induced myocardial ischaemia than in those without. Exercise-induced electrocardiographic myocardial ischaemia, however, is not associated with exaggerated BNP secretion.

B-type natriuretic peptide (BNP) and N-terminal proBNP fragment (NT-proBNP) are increased in coronary heart disease (CHD), and the increase in these peptides may be directly related to the severity of CHD.[1–4] It has been suggested that patients with CHD have exaggerated BNP or NT-proBNP secretion during transient myocardial ischaemia,[4–10] but this is controversial.[1 11–12]

The exercise electrocardiographic tolerance test (ETT) remains a cornerstone in the diagnosis of CHD, as it is commonly available and cost effective. There are, however, few data on BNP and NT-proBNP in relation to the ETT. If, however, proved to be of value, NT-proBNP might be useful in the assessment and management of patients with CHD.

We, therefore, measured serum NT-proBNP before and after an ETT to investigate whether increased exercise-induced NT-proBNP secretion is a feature of symptomatic exercise-induced electrocardiographic myocardial ischaemia.

## MATERIAL AND METHODS

### Patients

Patients undergoing an ETT were recruited from a rapid access chest pain clinic. All patients presented with chest pain. Exclusion criteria included previous myocardial infarction, unstable angina, cardiac surgery, uncontrolled hypertension, heart failure and renal impairment. Patients gave written consent to participate in this study, which was approved by the Wolverhampton District Local Research Ethics Committee.

Patients were instructed to omit treatment on the day of the ETT. A resting blood sample was collected into gel tubes (Sarstead Monovet 4.7 ml, Z GEL, Sarstedt, Numbrecht, Germany), after which patients underwent an exercise test according to a standard Bruce protocol.[13] Another blood sample was collected 15 min after exercise. Samples were separated within 60 min and serum frozen at −80℃ until assayed for NT-proBNP.

### Analytical methods

NT-proBNP was measured by electrochemiluminescence immunoassay (Elecys proBNP, Roche Diagnostics GmbH, Mannheim, Germany) on the Roche Modular Analytics E170 immunoassay analyser. The assay has a detection limit of 5 ng/l. The intra-assay and interassay coefficients of variation for the NT-proBNP assay are 0.9% and 5.8%, respectively.

### Statistical analysis

Raw data were non-parametric; however, data were normally distributed after logarithmic transformation. The importance of within-group and between-group continuous logarithmic variables was, therefore, assessed by paired t test and unpaired t test with Welch correction, respectively. Dichotomous variables were assessed by Fisher's exact test. Statistical analyses were carried out using GraphPad Instat V.3.00 for Windows 95. Results are expressed in their pretransformed form as mean (SD).

## RESULTS

We studied 14 patients with a positive ETT and 45 patients with a negative ETT, who served as controls. Those with a positive ETT developed chest pain during the ETT. Table 1 shows the clinical characteristics and serum NT-proBNP results of both groups.

In summary, although matched for age, there were more women in the ETT-negative group. Serum NT-proBNP concentrations before and after exercise were higher ($p<0.05$) in patients with positive ETT than patients with negative ETT. After exercise, serum NT-proBNP concentrations increased ($p<0.001$) in both groups, but the incremental increase in serum NT-proBNP concentrations were similar in both groups.

## DISCUSSION

The higher baseline and post-exercise serum NT-proBNP concentrations in patients with positive ETT than in controls confirms increased BNP secretion in patients with CHD.[1–4] In this study, however, exercise-induced NT-proBNP secretion was similar in patients with positive ETT and in patients with negative ETT.

**Abbreviations:** BNP, B-type natriuretic peptide; CHD, Coronary heart disease; ETT, electrocardiogram test; NT-proBNP, N-terminal proBNP

**Table 1** Demographics of patients with and without myocardial ischaemia and their serum N-terminal proB-type natriuretic peptide concentrations during an exercise echocardiograph test

| | Positive exercise ECG | Negative exercise ECG | p Value |
|---|---|---|---|
| Number | 14 | 45 | |
| Sex, M/F | 11/3 | 16/29 | 0.030 |
| Age (years) | 60.9 (11.8) | 57.2 (13.8) | 0.340 |
| Systolic BP (mm Hg) | 145.9 (14.4) | 137.0 (19.8) | 0.106 |
| Diastolic BP (mm Hg) | 84.1 (12.7) | 83.9 (10.6) | 0.997 |
| Resting heart rate (beats/min) | 75.5 (12.3) | 75.4 (11.6) | 0.999 |
| Maximum heart rate (beats/min) | 141.6 (16.9) | 149.1 (22.7) | 0.266 |
| Maximum metabolic equivalents | 5.97 (0.65) | 9.17 (3.30) | 0.002 |
| Time exercised (min) | 4.1 (2.85) | 9.1 (3.2) | 0.004 |
| Pre-exercise NT-proBNP (ng/l) | 71.4 (41.2) | 54.0 (61.2) | 0.013 |
| Post-exercise NT-proBNP (ng/l) | 76.8 (44.0)* | 60.1 (69.0)* | 0.020 |
| Increase in NT-proBNP (ng/l) | 4.7 (4.2) | 6.2 (8.6) | 0.619 |

BP, blood pressure; ECG, electrocardiogram; F, female; M, male; NT-proBNP, N-terminal proB-Type natriuretic peptide.
*$p<0.001$ compared with pre-exercise.
Results are raw pretransformed data expressed as mean (SD).

Our study is in agreement with that reporting higher BNP concentrations but similar incremental BNP concentrations in patients with myocardial ischaemia compared with controls,[11] but differs from that reporting similar NT-proBNP concentrations in patients with and without electrocardiographic myocardial ischaemia,[12] and also differs from those reporting increased incremental BNP responses in those with myocardial ischaemia compared with controls.[4–10]

The results in our study are partly different from those reported in the only other comparable study.[12] Weber *et al*[12], similarly reported no difference in incremental serum NT-proBNP concentrations between patients with and without electrographic myocardial ischaemia, but unlike us they also reported similar baseline and post-exercise NT-proBNP concentrations in both study groups.

The differences in these studies could be because of different study groups, different durations and intensities of exercise, different techniques for diagnosing myocardial ischaemia, different analytical techniques and type-1 and type-2 statistical errors.

Serum NT-proBNP may be affected by age, sex and heart rate.[14] In our study, groups were matched for age and heart rate, but 21% of patients with a positive ETT were women compared with 36% in the control group. The higher NT-proBNP in those with symptomatic myocardial ischaemia is not explained by sex, as NT-proBNP is higher in women than men.[14] In this study, compared with controls, patients with a positive ETT had reduced exercise capacity limited by symptomatic exertion-induced myocardial ischaemia; although not practical it is, however, possible that if patients with a positive ETT had exercised for the same duration and intensity as controls, there may have been a significant between-group difference in incremental NT-proBNP results.

In summary, we confirm that patients with symptomatic CHD have increased serum NT-proBNP concentrations. We found no evidence to support the notion that exaggerated exercise-induced BNP excretion is associated with reversible exertion-induced electrocardiographic myocardial ischaemia.

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Competing interests: None.

Ethical approval: The Wolverhampton District Local Research Ethics Committee approved the study.

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